UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/217,780	03/25/94	WOZNEY	I GI5202CIP

EXAMINER	
JACOBSON, D	
ART UNIT	**PAPER NUMBER**
1814	8

18M2/0112

LEGAL AFFAIRS DEPARTMENT
GENETICS INSTITUTE INC
87 CAMBRIDGEPARK DRIVE
CAMBRIDGE MA 02140

DATE MAILED: 01/12/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication (election) filed on 11/14/94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~days~~ from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-28 are pending in the application.
   Of the above, claims 14-21, 24-28 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-13, 22, 23 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Applicant's election without traverse of Group I, claims 1-13, 22, and 23 in Paper No. 7 is acknowledged.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e., failing to provide an enabling disclosure.

The specification describes expression of the V1-1 protein, as encoded by SEQ ID NO. 1, in bacterial and eukaryotic host cells using vectors that contain known regulatory sequences. SEQ ID NO. 1 consists of the mature V1-1 protein with what appears to be a propeptide sequence. However, applicants have not shown that this region encodes a complete and/or functional propeptide or leader sequence. The V1-1 propeptide sequence is not deemed to be enabled. The specification also fails to disclose the sequences of propeptide sequences from other BMP or TGF-beta proteins. The specification does not teach expression of V1-1 using vectors containing a heterologous propeptide, i.e., a

propeptide from a member of the TGF-beta superfamily. It is not known how the inclusion of such propeptide sequences would affect expression and/or activity of the V1-1 protein. Applicants have not provided sufficient guidance so that one of skill in the art could express V1-1 using a propeptide sequence. Thus, chimeric DNA molecules and methods of use to produce the V1-1 protein are not enabled by the specification.

Applicants traverse this rejection as made in parent application 08/164,103 on the grounds that the specification teaches that the sequences of numerous BMP proteins and other TGF-beta proteins are known in the art. As discussed above, the specification does not teach specific propeptide sequences. Numerous different BMP and TGF-beta proteins are known in the art and, although they share some sequence homology, they have distinct sequences. Applicants have not shown that the disclosed proteins could be successfully expressed using heterologous propeptide sequences. It is unknown if propeptide sequences would be correctly removed during protein maturation or if they might interfere with protein processing. Applicants have shown that BMPs may be expressed when ligated to heterologous BMP propeptide sequences (U.S. Pat. 5,168,050). However, there is no evidence that other TGF-beta propeptide sequences would also be effective. Due to the numerous possible propeptide sequences and the unpredictable nature of the art, it would require undue

experimentation to construct and screen all of the possible TGF-beta superfamily propeptide sequences that may be used in the expression of the disclosed V1-1 proteins.

In addition, claim 3 is drawn to a V1-1 related protein which exhibits the ability to form cartilage and/or bone. The specification defines the V1-1 proteins as "tendon/ligament-like tissue inducing proteins" (page 2, lines 4-7). The specification does not describe the V1-1 proteins as having cartilage and/or bone formation activity. Proteins having such activity are not enabled by the specification.

Claims 3, 6, 12, 22, and 23 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-6, 22, and 23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 22 are indefinite in their recitation of "V1-1 related protein" because the nature and identity of this protein is unknown. The specification discloses a V1-1 protein as one having the ability to induce the formation of tendon tissue. However, the chemical nature, i.e., size, charge, structure, etc., is uncertain. Claims depending on claims 1 and 22 are also

deemed to be indefinite. This rejection may be overcome by amending the claims to recite a specific sequence, such as in claims 2, 3, and 7.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-13 are rejected under 35 U.S.C. § 102(a) as being anticipated by Neidhardt et al. (WO 93/16099).

Neidhardt et al. describe the human MP52 protein that is related to the TGF-beta family of proteins. The reference also describes the DNA sequence of MP52 and expression thereof using recombinant means. The protein of Neidhardt et al. and the DNA sequence encoding are 80% homologous to applicants' V1-1 protein. The instant claims are written so broadly as to encompass the MP52 protein of Neidhardt et al. and are anticipated by the reference. It is noted that, although Neidhardt et al. do not teach that the MP52 protein exhibits the ability to form tendon/ligament-like tissue, there is no showing that MP52 does not have this activity. The instant claims are drawn to DNA molecules that are significantly homologous to the protein of

Neidhardt et al. This rejection may be overcome by a showing that MP52 does not induce tendon/ligament formation.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-13 and 22-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 and 22-23 of copending application Serial No. 08/164,102. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed DNA sequences are the same. The claims of the instant application are drawn to a DNA encoding a "V1-1 related protein". The claims of the copending application are drawn to a "V1-1 protein". However, the claims of both applications are drawn to the same DNA sequences, vectors, cells,

and recombinant methods of producing the V1-1 proteins. The claims are thus not seen to be patentably distinct.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted in applicants' preliminary amendment that 08/164,103 is abandoned. As of the date of the present Office action this application was still pending.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dian C. Jacobson whose telephone number is (703) 308-2973. The examiner can normally be reached Monday-Thursday 8:00 to 5:00. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at (703) 308-4216. The FAX number for this Group is (703) 308-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Dian C. Jacobson

DIAN C. JACOBSON
PATENT EXAMINER
GROUP 1800